Improved Accuracy of Percutaneous Biopsy Using "Cross and Push" Technique for Patients Suspected with Malignant Biliary Strictures

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Abstract

Introduction: Various methods have been used to sample biliary strictures including percutaneous fine-needle aspiration biopsy, intraluminal biliary washings and cytological analysis of drained bile. However, none of these methods have proven to be particularly sensitive in the diagnosis of biliary tract malignancy. We report improved diagnostic accuracy using a modified technique at percutaneous transluminal biopsy in these patients.

Materials and Methods: 52 patients with obstructive jaundice due to a biliary stricture underwent transluminal forceps biopsy using flexible biopsy forceps kit commonly used for cardiac biopsies using a modified ‘cross and push’ technique. This entailed crossing the stricture with a 0.038-inch wire leading all the way down into the duodenum. A standard or long sheath was subsequently advanced up to the stricture over the wire. A Cook 5.2Fr biopsy forceps alongside the wire was introduced and the cup opened on exiting the sheath. With the biopsy forceps open, within the stricture, the sheath was used as a pusher to advance biopsy cup into the stricture before the cup was closed and sample obtained. The data was analysed retrospectively.

Results: We report outcomes using this technique on 52 consecutive patients with obstructive jaundice secondary to a biliary stricture. The sensitivity and accuracy were 93.3% and 94.2% respectively. There was one procedure related late complication.

Conclusion: We propose the modified ‘cross and push’ technique to be a feasible, safe and a more accurate option over the standard technique for

sampling strictures of the biliary tree.

Introduction:

Ultrasound (US) guided fine needle aspiration (FNA) biopsies [1, 2] and automated biopsy gun samples [3] have yielded improved sensitivity and specificity for several sites in the body except the biliary tree. Sampling the biliary tree in suspected malignant obstruction has historically proven problematic and is thought to be for two main reasons. Firstly, the tumours are often small and visualisation as a biopsy target by ultrasound is technically difficult or impossible [4]. Secondly, these tumours are often accompanied by a significant desmoplastic response making any sort of sampling unreliable [5-7].

Endoluminal techniques employed for obtaining biliary samples can be broadly divided into those that require a percutaneous or endoscopic access tract. Percutaneous based methods include percutaneous transhepatic cholangiogram (PTC) brush cytology and cholangioscopy [8] whereas endoscopic based methods include endoscopic retrograde cholangio-pancreatography (ERCP) and endoscopic ultrasound (EUS).

Whilst EUS-FNA in recent years has become an established method for pancreatic lesions with sensitivities approaching 100%, it is less sensitive (79%) for hilar strictures [9, 10]. On obtaining access to the biliary tree in either ERCP and PTC based methods either washings or brushings can be taken and sent for cytology. Brush cytology has been popular and probably the most used method despite its low yield of specimen and variable accuracy, with studies showing sensitivities ranging from 30 – 75% [11-13].

Since the 1980's biopsy forceps have been used via the percutaneous tract to sample the biliary tree and obtain histology in suspected malignant obstruction as reported by a few centres [14]. Two smaller studies with less than 25 patients, showed a wide range of sensitivity as low as 30% [15] and up to 100% [16]. Jung et al reported the only large study comprising 130 patients where they employed a specific type of forceps (Cordis, Miami, Florida) to obtain biopsy samples demonstrating a sensitivity of 78.4% [17]. Tapping et al reported cytological sampling versus forceps biopsy during percutaneous transhepatic biliary drainage in 119 patients with suspected malignant inoperable obstructive jaundice. Histological diagnosis after forceps biopsy was more successful than cytology: Sensitivity was 78 versus 61%, and negative predictive value was 30 versus 19%. Cytology results were never positive when the forceps biopsy was negative [18].

We evaluated our results based on a modified biopsy technique to sample biliary strictures in patients with suspected malignant biliary obstruction.

Materials and Methods:

We have retrospectively reviewed 52 consecutive patients who had a biliary stricture biopsy performed by a single hepatobiliary interventional radiologist between Oct. 2007 and March 2012 at a major hepatobiliary centre, using the 'cross and push' technique. The decision for PTC ± drainage was made for all of these patients presenting with obstructive jaundice suspected secondary to a malignant obstruction, following approval at a multi-disciplinary team review at our institution. This study reports sensitivity, specificity and accuracy of this

method of biliary sampling as well as a record of any complications encountered during or after the procedure as a result of the biopsy.

Technique:

All procedures were performed under intra-venous sedo-analgesia and local anaesthesia at the puncture site. Initial percutaneous access to the biliary system was achieved with a 21-guage access system (AccuStick™ Boston Scientific, MA) followed by an exchange of this access to a 0.038-inch system in conventional fashion under ultrasound and fluoroscopic guidance. A cholangiogram to identify the level of obstruction was performed and access to the biliary tree secured using a standard (11cm length) 7 Fr Brite-tip sheath (Cordis™, Miami, FL) or a long (23cm length) 7 Fr sheath (Cordis™, Miami, FL). Thereafter attempts were made to cross the biliary stricture using standard interventional radiology techniques with a variety of catheters and wires. It is imperative to cross the stricture with a 0.038-inch wire leading all the way down into the duodenum. The sheath is then advanced over the wire up to the proximal limit of the stricture. A flexible cup biopsy forceps (Cook 5.2 Fr 60cm myocardial biopsy forceps with a standard sized (2.25cc) cup (Cook™, Bloomington, IN)) was then passed through the sheath alongside the guide wire. The cup was opened on exiting the sheath with the tip of the sheath remaining resident just proximal to the stricture. With the biopsy forceps open in this manner, within the stricture, we then used the sheath as a pusher to advance the open biopsy forceps into the stricture before the cup was closed and sample obtained (Fig. 1a). Up to five samples were taken and sent for histology. The sheath always

remained *in-situ* to allow safe exchange of the biopsy forceps between each samples. The procedure was completed with a control cholangiogram following placement of a biliary drain or a metallic stent in a conventional manner.

The modified ‘cross and push technique’ was employed in 52 patients. Data was collected retrospectively recording age, sex, pre-biopsy liver functions, biopsy characteristics, location and histology of lesion. The data is presented including results of final diagnosis and complications. Probability of survival was determined using the Kaplan-Meier method. Correlation of biopsy results to final diagnosis was established either through subsequent follow-up (both radiological and clinical) or surgical histology. 2 X 2 table statistics were performed to derive sensitivity, specificity, positive (PPV) and negative (NPV) predictive value; and accuracy.

Results:

52 patients who presented with obstructive jaundice presumed secondary to a suspected malignant stricture in the biliary tree based on clinical presentation and findings at PTC cholangiogram were included in the study. The results are presented in Table 1. All biopsies had samples reliable to make a histologic diagnosis. None of the samples obtained were found to be suspicious, inadequate, necrotic or with fibrinous materials. There were 4 (8%) crush artefacts but despite this the cyto-pathological assessment was possible as the largest dimension amongst these samples was 1-2 mm. 42 of the fifty-two (81%) biopsies resulted in a correct diagnosis of malignancy. The specific histologic diagnosis correlated with the clinical diagnosis in 49 cases (accuracy - 94.2%).

The remaining three cases were confirmed to have an underlying malignancy (false negatives), although the exact histologic type was on PTC biopsy was reported as benign (inflammatory changes). One of these three patients had strictures secondary to a primary gall-bladder carcinoma and the other two had primary gastric and colo-rectal cancers each, causing extrinsic compression of the biliary tree from lymph node secondaries. There were seven true negative diagnoses. There were no false-positive diagnoses. For the diagnosis of malignant biliary obstruction, transluminal forceps biopsy using ‘cross and push’ technique had a sensitivity of 93.3% and a specificity of 100%. Although the positive predictive value was 100%, the negative predictive value was only 70%. Median overall survival in patients with malignant biliary strictures following primary decompression and histology was 4.8 months.

We noticed one procedure related complication. The patient presented with haemobila two months post procedure. CT showed a hepatic artery pseudoaneurysm located in the periphery of the liver at the access point from the PTC. This was anatomically distant from the biopsy site, which was at the distal CBD. It was treated successfully with embolisation.

Discussion:

We report an accurate and safe ‘technical note’ to sample the biliary tree in suspected malignant obstruction using readily available kit.

We favoured the 5.2 Fr flexible biopsy forceps and used it for all patients as it permitted its deployment alongside a guide wire within the sheath. We recommended biopsy forceps to be advanced inside a long 7 Fr sheath with the

tip placed in the stricture (Fig 2a, b). This is possible alongside a 0.038-inch wire after the stricture has been crossed. It seems logical that the leading edge of the sheath can aid pushing an open cup of the biopsy forceps into the substance of the stricture (Fig 1a) thereby resulting in better sampling. We believe retro-flexion (Fig 1b) of the biopsy cups results in a poor tissue yield and could be prevented by deploying the ‘cross and push’ technique.

The procedure related complication (hepatic pseudoaneurysm) was due to the PTC access and not the biopsy as it was anatomically distant. Such complications are well reported in patients who have a PTC alone, hence we believe it is not solely due to the biopsy technique [20].

We recognise differentiating true from false negatives is difficult. Overall there were 10 patients with a negative biopsy for malignancy of which 3 (5.7%) were regarded as false negatives. This was on the basis of clinical and radiological corroboration during subsequent follow-up and histocytopathological evidence where available. The overall limitations of the modified technique lie in the low negative predictive value of 70%. However, given the nature of the disease process and desmoplastic response associated with cholangiocarcinoma a higher false negative rate may be expected. Extrinsic compression of biliary tree, which is usually extrahepatic, is generally managed by ERCP and stenting at our institution and hence we had only 2 patients. In both cases the percutaneous endoluminal biopsy (PTEB) histology obtained was benign. We also recognise such patients are more prone to get a false negative result and hence the biopsy results are unreliable in extrinsic lesions [21]. We also noticed

some crush artefacts but achieved decent quality histology in spite of small cup size. We believe our modified technique is more sensitive with better accuracy than FNA biopsy [22], bile cytology [23], brush cytology [11-13] and previously described forceps biopsy techniques [8, 18] for sampling the biliary tree in obstructive jaundice. Patients often present with severe liver dysfunction and the referring institution usually achieves drainage of the biliary tree. We believe a rapid diagnosis is imperative in patients suspected with malignant strictures, as overall survival is poor.

The overall sensitivity of the techniques reported here was comparable with the largest reported study employing intra-luminal forceps biopsies to sample the biliary tree [17]. However our modified technique yielded better sensitivity and accuracy of sampling suspected malignant biliary strictures. The reluctance to pursue a histological confirmation in all cases is understandable. NCCN guidelines do recommend biopsy in certain situations [19]. However, we are in favour of a biopsy whenever possible in patients presenting with suspected malignant biliary obstruction based on clinical, imaging and laboratory criteria for the following reasons. Firstly, we have found a 13.5% incidence of true negative in cases presumed to be malignant (Table 1). Secondly, 8% cases had unexpected malignant histology such as NET, HCC and CRM which had an entirely different course of therapy. Finally, histological confirmation may be required to enrol patients in appropriate clinical trials. Hence we recommend that this modified technique be employed in all cases where PTC is undertaken for suspected bile duct malignancy.

n	52
Mean Age in years (95%CI)	68.8 (+/-3)
Age range (years)	38.2 – 87.8
Male: Female ratio	1.9:1
Mean Pre-Biopsy liver functions (95%CI)	
Bilirubin (umol/L)	284 (+/-50)
GGT (IU/L)	330 (+/-91)
AST (IU/L)	119 (+/-25)
ALT (IU/L)	119 (+/-28)
ALP (IU/L)	1562 (+/-326)
Biopsy characteristics	
Median number of Cores	3
Median length of cores (mm)	2
Crush artefacts	4/52 (8%)

Histology and Location of stricture		**Intra-hepatic**		**Extra-hepatic**			
Benign Histology on PTEB (True negatives)	*n = 7*	**Hilar**	**Main RHD**	**Distal CBD**	**Mid CBD**	**Proximal CBD**	**BEA**
Benign (all inflammatory)	7	1		3	1	1	1
Benign Histology on PTEB (False negatives)	*n = 3*						
Solitary metastasis from previously resected gastric adenocarcinoma	1			1			

Solitary metastasis from previously resected gall bladder adenocarcinoma	1	1					
de novo Colorectal Metastasis (CRM)	1	1					
Malignant Histology on PTEB	*n = 42*	**Hilar**	**Main RHD**	**Distal CBD**	**Mid CBD**	**Proximal CBD**	**BEA**
Cholangiocarcinoma	28	17	1	5	1	4	
Pancreatic Adenocarcinoma	11	2		9			
Hepatocelluar Carcinoma (HCC)	1	1					
Neuroendocrine Tumour (NET)	2	2					

Test reliability to pick up malignant biliary strictures	
Sensitivity (%)	93.3
Specificity (%)	100
Positive Predictive Value (%)	100
Negative Predictive Value (%)	70
Accuracy (%)	94.2
Procedure related complication	1 (Hepatic artery pseudo-aneurysm
Median Follow up (months)	8.5
Median Overall Survival (months) since biopsy with benign histology	31.0
Median Overall Survival (months) since biopsy with malignant histology	6.8

Table 1: Patient characteristics and overall data.

(* False Negatives; RHD – Right hepatic duct; CBD – Common Bile Duct; BEA – Biliary Enteric Anastomosis)

Conflict of Interest Statement

Prashant Patel: No conflict of interest

Balaji Rangarajan: No conflict of interest

Kamarjit Mangat: recieved professional fees from Cook™, Bloomington, IN., to present the study findings at the CIRSE 2012 and SIR 2013 meetings. Cook Medical has patented a Transluminal Biliary Biopsy Forceps Set (BBFS-100) with royalties paid to Kamarjit Mangat.

Statement of Informed Consent

Informed consent was obtained from all individual participants included in the study.

Statement of Human and Animal rights

The reported study is a technical note and did not require ethics committee approval. The study was logged as an Institutional audit.

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